

## REMARKS

### Introductory Matters

Claims 1-11, 14, 16-17, 20, 22 and 27 are pending in this application. Claims 1-11, 14, 16-17, 20, 22 and 27 stand rejected.

Applicants have canceled claim 11.

Applicants have amended claim 1, changing the definition of R<sup>x</sup> to hydrogen only. Support for this amendment can be found in the specification as originally filed (see e.g., page 140, line 4 to page 141, line 23).

Applicants have amended the definition of R<sup>8</sup> to remove halo.

These amendments add no new matter.

## THE OFFICE ACTION

### 35 U.S.C. § 112, first paragraph

Claims 11 stands rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. The Examiner contends that the specification "while being enabling for the treatment of colon cancer, does not reasonably provide enablement for the treatment of all other diseases embraced by the instant claims." Applicants traverse. Nevertheless, to expedite prosecution, applicants have canceled claim 11, thus obviating the rejection.

### 35 U.S.C. § 103

Claims 1-11, 14, 16-17, 20, 22 and 27 stand rejected under 35 U.S.C. § 103 as being obvious over Bradbury et al., WO 00/39101; Armistead et al., WO/01/60816; or Pease et al., WO 01/64655. The Examiner maintains his contention that "each of the references **individually** taught and disclosed compounds that are structurally analogous to the instantly claimed compounds." With respect to WO 01/39101, the Examiner contends that the reference differs from the instant claim by the position of the substituent, and thus the compounds are positional isomers. With respect to WO 01/60816, the Examiner contends that the compounds differ by a -CH<sub>2</sub>- group, and thus are structural homologues. The Examiner cites several CCPA cases, asserting that "compounds that are structurally analogous to prior art compounds are *prima facie* obvious absent a showing of unexpected results."

Applicants traverse. However, to expedite prosecution, applicants have amended claim 1, changing the definition of R<sup>x</sup> to hydrogen. Applicants have also removed halo from the definition of R<sup>8</sup>. Applicants respectfully submit that the amended claims are not prima facie obvious in light of Bradbury et al., WO 00/39101; Armistead et al., WO 01/60816; or Pease et al., WO 01/64655.

With respect to WO 00/39101 and WO 01/64655, the Examiner contends that the compounds of the instant claims, which can be substituted in the 6-position (R<sup>y</sup>) with halo, are prima facie obvious over certain compounds in WO 00/39101 and WO 01/64655, which are substituted in the 5-position (R<sup>x</sup>) with a bromo group. The Examiner contends that the compounds are positional isomers. Applicants traverse.

Applicants respectfully submit that compounds of the cited references are not positional isomers of the compounds of the amended claims. Applicants have amended claim 1 by removing halo from the definition of R<sup>8</sup>. Accordingly, R<sup>y</sup>, which is defined as T-R<sup>8</sup>, does not include bromo. As a result, the compounds of the cited references, which contain bromo at the 5-position, are not positional isomers of the compounds of the amended claims, which do not contain bromo in either the 5- or 6- positions.

Additionally, the cited references teach away from the pyrazole compounds described in the instant claims. Unlike the compounds of the instant claims, which describe aminopyrimidines substituted with a pyrazole group, the vast majority of the compounds described in WO 01/64655 and WO 00/39101 are aminopyrimidines substituted with 6-membered aromatic groups (for phenyl, see WO 01/64655, Examples 1-90, 99-100, 101-113; see also WO 00/39101, Examples 1-117, 137-150, 162-193, 195-215, 225-234; for pyridine, see WO 01/64655, Examples 91-98, 114-117, see also WO 00/39101, Examples 118-133, 136, 151-158, 216-224). Only two compounds in each application (compounds 118-119 in WO 01/64655 and compounds 160-161 in WO 00/39101) contain pyrazoles. Accordingly, applicants respectfully submit that the instant claims are not prima facie obvious in light of WO 00/39101 and WO 01/64655.

With respect to WO 01/60816, applicants respectfully submit that the amended claims are nonobvious in light of the cited reference. The compounds of the instant claims are only substituted in the 6-position. Nothing in the prior art suggests substituting the aminopyrimidine specifically in the 6-position in order to enhance kinase activity. In fact, the prior art only describes aminopyrimidine that are unsubstituted in the 5- and 6- positions. The

Court in In re Wagner, 371 F.2d 877, 152 U.S.P.Q. 552 (C.C.P.A. 1967), reversed a PTO conclusion of obviousness based on structural similarity. In this case, the claims recited benzimidazole derivatives substituted at 2 specific positions. The prior art taught benzimidazole derivatives that were either unsubstituted or substituted at different positions. The CCPA rejected the PTO's conclusion of obviousness, stating that nothing in the prior art suggested substituting in the particular positions claimed "so as to enhance the biological or pharmaceutical activity of the compound." Similarly, nothing in the prior art suggests substituting the aminopyrimidine specifically in the 6-position in order to enhance kinase activity. Accordingly, applicants respectfully submit that the amended claims are nonobvious over WO 01/60816.

For all the above reasons, applicants respectfully request that the Examiner withdraw these 103 rejections.

#### CONCLUSION

Accordingly, applicants request that the Examiner enter the above amendments, consider the foregoing remarks, and allow the pending claims to issue.

If the Examiner believes that a telephone discussion would further issuance of this application, the Examiner is invited to call the undersigned attorney at any time.

Respectfully submitted,

/Jennifer G. Che/

Jennifer G. Che, Reg. No. 58,035  
Attorney for Applicants  
Lisa A. Dixon, Reg. No. 40,995  
Attorney for Applicants  
Vertex Pharmaceuticals Incorporated  
130 Waverly Street  
Cambridge, Massachusetts 02139  
Tel: (617) 444-6525  
Fax: (617) 444-6483  
**Customer No. 27916**